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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,475	RAMIREZ-VICK ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9 and 12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12 November 2003 has been entered.

Status of the Claims

2. This action is in response to papers filed 12 November 2003 in which claims 1, 4, 9 and 12. All of the amendments have been thoroughly reviewed and entered. The previous objection to the specification in the Office Action dated 12 August 2003 is maintained as reiterated below. The previous rejections under 35 U.S.C. 102(e) and 35 U.S.C. 103(a) are withdrawn in view of the amendments.

All of the arguments have been thoroughly reviewed and are discussed below as they apply to the new rejections. New grounds for rejection are discussed.

Claims 1, 4-9, 12-16 are under prosecution.

Specification

3. The amendment filed 12 November 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The attempt to incorporate subject matter into this application by reference to parent application 09/584,661 is improper because the incorporation by reference was not part of the specification as originally filed. While it is appropriate amend the specification to cross reference the parent application it is not appropriate to amend the specification to incorporate-by-reference the parent. Therefore, the incorporation by reference constitutes new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Response to Comments

4. Applicant states that the incorporation by reference statement is filed concurrently with the filing of the Request for Continued Prosecution and as such, does not add new matter. The statement is acknowledged. However, the instant application is an RCE. As such, the specification is the same as the specification filed with the original application having the same application number. ANY addition to that specification introduces new matter. A change in the specification or introduction of additional subject matter is only proper with the filing of a Continuation in Part. Because the instant application is an RCE, the addition of subject matter i.e. incorporation by reference of a parent application constitutes new matter.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 4 and 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999).

Regarding Claim 1, Blackburn et al disclose a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known sequence to a solid support selected from the group consisting of silicon, glass and metals (Column 14, lines 45-54) that is coated with a metal selected from silver, copper, gold, palladium and platinum (Column 15, lines 12-Column 16, line 24), providing target nucleic acid molecules labeled with paramagnetic beads having a diameter of from about 1nm (0.001μm) to about 200μm (Column 21, lines 55-59), attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets (Column 6, lines 30-60; Column 9, lines 31-61; Column 21, lines 20-65; and Column 38, line 61-Column 39, line13).

Blackburn et al specifically teach the paramagnetic labels having a diameter of from about 1nm (0.001μm) to about 200μm (Column 21, lines 55-59). They do not specifically teach the claimed diameter range of from about 1 nm to 10nm.

However, the courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not

overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.). Therefore, the claimed range of from about 1 nm to 10nm is prima facie obvious in view of overlapping range taught by Blackburn et al.

Regarding Claim 4, Blackburn et al disclose the method wherein the paramagnetic labels comprise superparamagnetic particles i.e. a diameter of from about 1 to about 10 nanometers (Column 21, lines 32-59). The specification defines superparamagnetic particles as those having a diameter of from about 1 to about 10nm. Because Blackburn teach these diameters, they teach superparamagnetic particles as defined by the specification.

Regarding Claim 7, Blackburn et al disclose the method wherein the nucleic acids are oligonucleotides, genomic DNA, cDNA, RNA or fragments thereof (Column 9, lines 11-30).

Regarding Claim 8, Blackburn et al disclose the method wherein at least one of the probe and target is labeled with a fluorescent detection molecule (Column 78, lines 25-35).

7. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999) as applied to Claim 1 above and further in view of Roelant (U.S. Patent No. 6,001,573, filed 23 October 1997).

Regarding Claim 5, Blackburn et al disclose a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known

sequence to a solid support, labeling nucleic acid target molecule with paramagnetic beads, attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets (Column 6, lines 30-60; Column 9, lines 31-61; Column 21, lines 20-65; and Column 38, line 61-Column 39, line13) wherein the magnetic beads are those known in the art (Column 21, lines 48-50) but they do not specifically teach the magnetic beads comprising porphyrins.

Roelant teach a similar method of nucleic acid hybridization comprising attaching probe molecules to a solid support; labeling target molecules with paramagnetic labels; contacting the labeled molecules with the solid support; and detecting the hybridized target molecules wherein the paramagnetic labels comprise paramagnetic porphyrins (Column 5, line 66-Column 6, line 16) wherein the porphyrin label provides a universal label which attaches irreversibly without bridging agents and can be detected in an amount which is proportional to the number of labeled particles (Column 3, lines 59-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to label the paramagnetic beads of Blackburn et al with the porphyrin label taught by Roelant for the expected benefit of irreversible attachment of the label and for the additional benefit of quantifying target simply by quantifying the label as taught by Roelant (Column 3, lines 59-65).

8. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999) in view of Basalt (U.S. Patent No. 5,981,297).

Regarding Claims 6 and 14, Blackburn et al disclose a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known sequence to a solid support, labeling nucleic acid target molecule with paramagnetic beads, attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets (Column 6, lines 30-60; Column 9, lines 31-61; Column 21, lines 20-65; and Column 38, line 61-Column 39, line13) wherein the nucleic acids are attached to the paramagnetic beads using known techniques (Column 19, lines 58-59) but they do not specifically teach cleavable conjugating attachment. However, Basalt teaches a similar method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules of known sequence (i.e. binding molecules capable of undergoing selective binding with a target species, Column 4, lines 20-24)to a solid support; labeling nucleic acid target molecules with paramagnetic labels; contacting the labeled target molecules with the solid support; activating a magnetic field whereby the labeled molecules are attracted to the solid support (Column 7, lines 21-37); washing the support and inverting the polarity of the magnetic field to remove any unbound or non-specifically bound molecules; and detecting the hybridized target nucleic acid molecules (Column 3, line 39-Column 4, line 8 and Column 7, lines 21-64) wherein the paramagnetic labels are attached to the nucleic acid molecules using cleavable conjugating molecules i.e. selective binding molecules in a sandwich-type assay e.g. DNA tags (Column 4, lines 9-28 and Column 9, lines 16-33). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the cleavable nucleic acid-bead attachment of Basalt to the method of Blackburn et al thereby

maximizing the number of targets detected with the least number of attachments as taught by Basalt (Column 9, lines 21-32).

9. Claims 9, 12 and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999) in view of Brown et al (U.S. Patent No. 5,807,522, filed 7 June 1995).

Regarding Claim 9, Blackburn et al disclose a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known sequence to a solid support selected from the group consisting of silicon, glass and metals (Column 14, lines 45-54) that is coated with a metal selected from silver, copper, gold, palladium and platinum (Column 15, lines 12-Column 16, line 24), providing target nucleic acid molecules labeled with paramagnetic beads having a diameter of from about 1nm (0.001μm) to about 200μm (Column 21, lines 55-59), attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets (Column 6, lines 30-60; Column 9, lines 31-61; Column 21, lines 20-65; and Column 38, line 61-Column 39, line13). Blackburn et al teach that the probe and target are both nucleic acids (Column 9, lines 31-61) but they do not specifically teach their method wherein the target is immobilized and the probe is labeled. However, Brown et al teach a similar method wherein the target is immobilized and the probe is labeled whereby a plurality of patient samples are simultaneously analyzed on the same solid support (Column 15, lines 19-

47). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the target immobilization of Brown et al to the immobilized hybridization of Blackburn et al to thereby analyze a plurality of sample targets simultaneously for the expected benefit of rapid and convenient sample screening as taught by Brown et al (Column 15, lines 59-67).

Blackburn et al specifically teach the paramagnetic labels having a diameter of from about 1nm (0.001μm) to about 200μm (Column 21, lines 55-59). They do not specifically teach the claimed diameter range of from about 1 nm to 10nm.

However, the courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.). Therefore, the claimed range of from about 1 nm to 10nm is prima facie obvious in view of overlapping range taught by Blackburn et al.

Regarding Claim 12, Blackburn et al disclose the method wherein the paramagnetic labels comprise superparamagnetic particles i.e. a diameter of from about 1 to about 10 nanometers (Column 21, lines 32-59). The specification defines superparamagnetic particles as those having a diameter of from about 1 to about 10nm. Because Blackburn teach these diameters, they teach superparamagnetic particles as defined by the specification.

Regarding Claim 15, Blackburn et al disclose the method wherein the nucleic acids are oligonucleotides, genomic DNA, cDNA, RNA or fragments thereof (Column 9, lines 11-30).

Regarding Claim 16, Blackburn et al disclose the method wherein at least one of the probe and target is labeled with a fluorescent detection molecule (Column 78, lines 25-35).

10. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999) in view of Brown et al (U.S. Patent No. 5,807,522, filed 7 June 1995) as applied to Claim 9 above and further in view of Roelant (U.S. Patent No. 6,001,573, filed 23 October 1997).

Regarding Claims13, Blackburn et al disclose a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known sequence to a solid support, labeling nucleic acid target molecule with paramagnetic beads, attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets (Column 6, lines 30-60; Column 9, lines 31-61; Column 21, lines 20-65; and Column 38, line 61-Column 39, line13) wherein the magnetic beads are those known in the art (Column 21, lines 48-50) but they do not specifically teach the magnetic beads comprising porphyrins.

Roelant teach a similar method of nucleic acid hybridization comprising attaching probe molecules to a solid support; labeling target molecules with paramagnetic labels; contacting the labeled molecules with the solid support; and detecting the hybridized target molecules wherein the paramagnetic labels comprise paramagnetic porphyrins (Column 5, line 66-Column 6, line 16) wherein the porphyrin label provides a universal label which attaches irreversibly without bridging agents and can be detected in an amount which is proportional to the number of labeled particles (Column 3, lines 59-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to label the paramagnetic

beads of Blackburn et al with the porphyrin label taught by Roelant for the expected benefit of irreversible attachment of the label and for the additional benefit of quantifying target simply by quantifying the label as taught by Roelant (Column 3, lines 59-65).

11. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999) in view of Brown et al (U.S. Patent No. 5,807,522, filed 7 June 1995) as applied to Claim 9 above and further in view of Basalt (U.S. Patent No. 5,981,297).

Regarding Claims 6 and 14, Blackburn et al disclose a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known sequence to a solid support, labeling nucleic acid target molecule with paramagnetic beads, attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets (Column 6, lines 30-60; Column 9, lines 31-61; Column 21, lines 20-65; and Column 38, line 61-Column 39, line13) wherein the nucleic acids are attached to the paramagnetic beads using known techniques (Column 19, lines 58-59) but they do not specifically teach cleavable conjugating attachment. However, Basalt teaches a similar method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules of known sequence (i.e. binding molecules capable of undergoing

selective binding with a target species, Column 4, lines 20-24)to a solid support; labeling nucleic acid target molecules with paramagnetic labels; contacting the labeled target molecules with the solid support; activating a magnetic field whereby the labeled molecules are attracted to the solid support (Column 7, lines 21-37); washing the support and inverting the polarity of the magnetic field to remove any unbound or non-specifically bound molecules; and detecting the hybridized target nucleic acid molecules (Column 3, line 39-Column 4, line 8 and Column 7, lines 21-64) wherein the paramagnetic labels are attached to the nucleic acid molecules using cleavable conjugating molecules i.e. selective binding molecules in a sandwich-type assay e.g. DNA tags (Column 4, lines 9-28 and Column 9, lines 16-33). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the cleavable nucleic acid-bead attachment of Basalt to the method of Blackburn et al thereby maximizing the number of targets detected with the least number of attachments as taught by Basalt (Column 9, lines 21-32).

Response to Arguments regarding Blackburn

12. Applicant argues that the beads of Blackburn are much larger than those instantly claimed. The argument has been considered but is not found persuasive because, as stated above, Blackburn et al specifically teach the paramagnetic labels having a diameter of from about 1nm (0.001μm) to about 200μm (Column 21, lines 55-59). They do not specifically teach the claimed diameter range of from about 1 nm to 10nm.

However, the courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see

MPEP, 2144.05 I.). Therefore, the claimed range of from about 1 nm to 10nm is *prima facie* obvious in view of overlapping range taught by Blackburn et al.

Applicant argues that the washing and magnetic field application steps of Blackburn are used only with their shuttle particles or mixing particles which they define as being much larger than the instantly claimed diameter range of from about 1 nm to 10nm. The argument has been considered but is not found persuasive for the reasons stated above i.e. Blackburn specifically teach their magnetic particles useful for their method have a diameter from about 1nm (0.001µm) to about 200µm (Column 21, lines 55-59) which encompass the claimed range. Therefore, the instantly claimed range is *prima facie* obvious in view of Blackburn.

Applicant further argues that Roelant nor Baselt provide the elements missing from Blackburn i.e. paramagnetic labels having a diameter of about 1nm to about 10nm. The argument has been considered but is not found persuasive for the reasons stated above regarding Blackburn.

13. Claims 1, 4, 6-9, 12, 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baselt (U.S. Patent No. 5,981,297, filed 5 February 1997) in view of Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999).

Regarding Claims 1 and 4, Baselt discloses a method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules of known sequence (i.e. binding molecules capable of undergoing selective binding with a target species, Column 4, lines 20-24)to a solid support; labeling nucleic acid target molecules with paramagnetic labels; contacting the labeled target molecules with the solid support; activating a magnetic field whereby the labeled

molecules are attracted to the solid support (Column 7, lines 21-37); washing the support and inverting the polarity of the magnetic field to remove any unbound or non-specifically bound molecules; and detecting the hybridized target nucleic acid molecules (Column 3, line 39-Column 4, line 8 and Column 7, lines 21-64) wherein the method operates faster than other techniques (Column 4,lines 35-38) but they do not teach attracting the target molecules to the support by activating a magnetic field effective to induce rapid migration of the labeled probes. However, Blackburn et al teach a similar method wherein the solid support is selected from the group consisting of silicon, glass and metals (Column 14, lines 45-54) that is coated with a metal selected from silver, copper, gold, palladium and platinum (Column 15, lines 12-Column 16, line 24) and providing paramagnetic beads having a diameter of from about 1nm (0.001µm) to about 200µm (Column 21, lines 55-59), wherein a magnetic field is activated to induced rapid migration of the labeled target to thereby concentrate the target at the probe and increase the rate of hybridization by 50 to 100 fold (Column 17, lines 58-63; Column 19, lines 29-65; and Column 21, lines 20-67). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Baselt by attracting the target to the support thereby concentrating the target as taught by Blackburn et al (Column 19, lines 29-65; and Column 21, lines 20-67) for the expected benefit of increasing the rate of hybridization by 50 to 100 fold (Blackburn et al (Column 17, lines 58-63) wherein the solid support is silicon (Column 6, lines 32-36) and wherein the solid support is coated with gold (Column 6, lines 47-50).

Blackburn et al specifically teach the superparamagnetic labels having a diameter of from about 1nm (0.001µm) to about 200µm (Column 21, lines 55-59). They do not specifically teach the claimed diameter range of from about 1 nm to 10nm.

However, the courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have

similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.). Therefore, the claimed range of from about 1 nm to 10nm is prima facie obvious in view of overlapping range taught by Blackburn et al.

Regarding Claim 4, Blackburn et al disclose the method wherein the paramagnetic labels comprise superparamagnetic particles i.e. a diameter of from about 1 to about 10 nanometers (Column 21, lines 32-59). The specification defines superparamagnetic particles as those having a diameter of from about 1 to about 10nm. Because Blackburn teach these diameters, they teach superparamagnetic particles as defined by the specification.

Regarding Claim 6, Baselt et al disclose the paramagnetic labels are attached to the nucleic acid molecules using cleavable conjugating molecules i.e. selective binding molecules (Column 4, lines 23-28).

Regarding Claim 7, Baselt et al disclose the nucleic acid molecules are oligonucleotides or DNA (Column 4, lines 3-5).

Regarding Claim 8, Blackburn et al disclose the method wherein at least one of the probe and target is labeled with a fluorescent detection molecule (Column 78, lines 25-35) whereby the labeled molecule is detected. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the fluorescent label of Blackburn et al to the method of Baselt et al for the obvious benefit of detecting the molecule as suggested by Blackburn (Column 78, line s25-35).

Regarding Claim 9, Baselt disclose a method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules to a solid support; labeling nucleic acid target molecules of known sequence (i.e. target species capable of selective binding, Column 4, lines 20-24) with paramagnetic labels; contacting the labeled target molecules with the solid support; activating a magnetic field whereby the labeled molecules are attracted to the solid

support (Column 7, lines 21-37); washing the support and inverting the polarity of the magnetic field to remove any unbound or non-specifically bound molecules; and detecting the hybridized target nucleic acid molecules (Column 3, line 39-Column 4, line 8 and Column 7, lines 21-64) wherein the method operates faster than other techniques (Column 4,lines 35-38) but they do not teach attracting the target molecules to the support by activating a magnetic field effective to induce rapid migration of the labeled probes. However, Blackburn et al teach a similar method wherein the solid support is selected from the group consisting of silicon, glass and metals (Column 14, lines 45-54) that is coated with a metal selected from silver, copper, gold, palladium and platinum (Column 15, lines 12-Column 16, line 24) and providing paramagnetic beads having a diameter of from about 1nm (0.001μm) to about 200μm (Column 21, lines 55-59), wherein a magnetic field is activated to induced rapid migration of the labeled target to thereby concentrate the target at the probe and increase the rate of hybridization by 50 to 100 fold (Column 17, lines 58-63; Column 19, lines 29-65; and Column 21, lines 20-67). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Baselt by attracting the target to the support thereby concentrating the target as taught by Blackburn et al (Column 19, lines 29-65; and Column 21, lines 20-67) for the expected benefit of increasing the rate of hybridization by 50 to 100 fold (Blackburn et al (Column 17, lines 58-63) wherein the solid support is silicon (Column 6, lines 32-36) and wherein the solid support is coated with gold (Column 6, lines 47-50).

Blackburn et al specifically teach the superparamagnetic labels having a diameter of from about 1nm (0.001μm) to about 200μm (Column 21, lines 55-59). They do not specifically teach the claimed diameter range of from about 1 nm to 10nm.

However, the courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257,

191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.). Therefore, the claimed range of from about 1 nm to 10nm is prima facie obvious in view of overlapping range taught by Blackburn et al.

Regarding Claim 12, Blackburn et al disclose the method wherein the paramagnetic labels comprise superparamagnetic particles i.e. a diameter of from about 1 to about 10 nanometers (Column 21, lines 32-59). The specification defines superparamagnetic particles as those having a diameter of from about 1 to about 10nm. Because Blackburn teach these diameters, they teach superparamagnetic particles as defined by the specification.

Regarding Claim 14, Baselt et al disclose the nucleic acid molecules are oligonucleotides or DNA (Column 4, lines 3-5).

Regarding Claim 15, Baselt et al disclose the nucleic acid molecules are oligonucleotides or DNA (Column 4, lines 3-5).

Regarding Claim 16, Blackburn et al disclose the method wherein at least one of the probe and target is labeled with a fluorescent detection molecule (Column 78, lines 25-35) whereby the labeled molecule is detected. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the fluorescent label of Blackburn et al to the method of Baselt et al for the obvious benefit of detecting the molecule as suggested by Blackburn (Column 78, lines 25-35).

Response to Arguments

14. Applicant argues that the references do not teach all of the claimed elements. The arguments have been considered but are not found persuasive for the reasons stated above.

15. Claims 5 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baselt (U.S. Patent No. 5,981,297, filed 5 February 1997) in view of Blackburn et al (U.S. Patent No. 6,264,825, filed 23 June 1999) as applied to Claims 1 and 9 above and further in view of Roelant (U.S. Patent No. 6,001,573, filed 23 October 1997).

Regarding Claims 13, Baselt and Blackburn et al teach the methods of Claim 1 and 9 as discussed above wherein the magnetic beads are those known in the art (Blackburn et al, Column 21, lines 48-50) but they do not specifically teach the magnetic beads comprising porphyrins.

Roelant teach a similar method of nucleic acid hybridization comprising attaching probe molecules to a solid support; labeling target molecules with paramagnetic labels; contacting the labeled molecules with the solid support; and detecting the hybridized target molecules wherein the paramagnetic labels comprise paramagnetic porphyrins (Column 5, line 66-Column 6, line 16) wherein the porphyrin label provides a universal label which attaches irreversibly without bridging agents and can be detected in an amount which is proportional to the number of labeled particles (Column 3, lines 59-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to label the paramagnetic beads of Baselt and Blackburn et al with the porphyrin label taught by Roelant for the expected benefit of irreversible attachment of the label and for the additional benefit of quantifying target simply by quantifying the label as taught by Roelant (Column 3, lines 59-65).

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878 until 13 January 2004. Starting

14 January 2004, the examiner's phone number will be (517) 272-0741. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196. Starting 14 January 2003, the receptionist telephone number will be (517)-272-0507.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
January 15, 2004